## A)

# **ATENT COOPERATION TREATY**

To:

From the	INTERNATIONAL	. BUREAU
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### **PCT**

#### **NOTIFICATION OF ELECTION**

(PCT Rule 61.2)

Assistant Commissioner for Patents United States Patent and Trademark Office

**Box PCT** 

Washington, D.C.20231 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 29 May 2000 (29.05.00)

International application No. PCT/US99/23252

International filing date (day/month/year) 05 October 1999 (05.10.99) Applicant's or agent's file reference

DEX-0046

Priority date (day/month/year) 05 October 1998 (05.10.98)

**Applicant** 

MACINA, Roberto, A.

1.	The designated Office is hereby notified of its election made:
	X in the demand filed with the International Preliminary Examining Authority on:
	01 May 2000 (01.05.00)
	in a notice effecting later election filed with the International Bureau on:
2.	The election X was
	was not
	made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).
	·

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Authorized officer

Pascal Piriou

Facsimile No.: (41-22) 740.14.35 Telephone No.: (41-22) 338.83.38

Form PCT/IB/331 (July 1992)

US9923252

International application No. PCT/US99/23252

	SSIFICATION OF SUBJECT MATTER		
	:Please See Extra Sheet. :Please See Extra Sheet.		
According t	o International Patent Classification (IPC) or to both	national classification and IPC	
	DS SEARCHED		
Minimum d	ocumentation searched (classification system followed	d by classification symbols)	
	424/1.49, 9.1, 130.1, 139.1, 152.1, 178.1, 182.1; 435/		
Documentat	ion searched other than minimum documentation to the	extent that such documents are included	in the fields searched
Electronic d	ata base consulted during the international search (na	me of data base and, where practicable	, search terms used)
	NTS (EAST/BRS), MEDLINE, EMBASE, BIOSIS, C ms: esbp, espbii, hesfii, hesf, lipophilin, estramustine		ognos?
C. DOC	UMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where ap	propriate, of the relevant passages	Relevant to claim No.
X,P	WO 98/56248 A1 (SMITHKLINE BEI 17 December 1998, pages 9 and 16.	ECHMAN CORPORATION)	1, 5, 6 and 9
			10
Y,P			
X	WO 98/21331 A1 (INCYTE PHARMA 1998, pages 21, 24, 26-28, 31 and 41	•	1, 5, 6 and 9
			10
Y		·	
X Furth	er documents are listed in the continuation of Box C		
•	ecial categories of cited documents:  cument defining the general state of the art which is not considered	"T" later document published after the int date and not in conflict with the app the principle or theory underlying th	lication but cited to understand
to	be of particular relevance	"X" document of particular relevance; th	
	rlier document published on or after the international filing date cument which may throw doubts on priority claim(s) or which is	considered novel or cannot be considered when the document is taken alone	
<del>- ::</del> :	and to establish the publication date of another citation or other social reason (as specified)	eye dominant of narticular relevance; th	
*O* do	cument referring to an oral disclosure, use, exhibition or other	considered to involve an inventive combined with one or more other suc being obvious to a person skilled in	h documents, such combination
the	cument published prior to the international filing date but later than priority date claimed	*A* document member of the same paten	
Date of the	actual completion of the international search	Date of mailing of the international sec	arch report
12 JANU	ARY 2000	1/1 FEB 200	
Name and a Commission Box PCT	mailing address of the ISA/US mer of Patents and Trademarks	Authorized officer	Cellin
	n, D.C. 20231	Telephone No. (703) 308-0196	/
Facsimile N	io. (703) 305-3230	1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 - 1 -	.*

International application No. PCT/US99/23252

Catagonia	Citation of document with indication when appropriate of the salayant accesses	Relevant to claim No
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
Y	Database EMBASE on STN, Elsevier Sci. B.V., SHIINA et al. 'Immunohistochemical analysis of estramustine binding protein with particular reference to proliferative activity in human prostatic carcinoma,' abstract, Prostate, 1997, Vol. 32, No. 1, pages 49-58.	1, 3, 5 and 6
<b>\</b>	PARKER et al. Prostatic steroid binding protein: gene duplication and steroid binding. Nature. 01 July 1982, Vol. 298, pages 92-94, see entire document.	1-6
A,P	ZHAO et al. Lipophilins: Human peptides homologous to rat prostatein. Biochem. Biophys. Res. Commun. 1999, Vol. 256, pates 147-155, especially page 147.	1-6
	·	
	·	·
		1

International application No. PCT/US99/23252

	A. CLASSIFICATION OF SUBJECT MATTER: IPC (6):						
	A61K 51/00, 49/00, 39/395; C12Q 1/ 00, 1/68; GO1N 33/53, 33/567, 33/574						
	A. CLASSIFICATION OF SUBJECT MATTER: US CL:						
	424/1.49, 9.1, 130.1, 139.1, 152.1, 178.1, 182.1; 435/4, 6, 7.1, 7.2, 7.21, 7.23, 960						

Form PCT/ISA/210 (extra sheet)(July 1992)\*



## INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: JANE MASSEY LICATA LAW OFFICES OF JANE MASSEY LICATA 66 E. MAIN STREET MARLTON, NJ 08053 Docket System Status Report Docket Book

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY **EXAMINATION REPORT** 

(PCT Rule 71.1)

Date of Mailing (day/month/year)

Applicant's or agent's file reference

**DEX-0046** 

IMPORTANT NOTIFICATION

International application No.

International filing date (day/month/year)

Priority Date (day/month/year)

**05 OCTOBER 1999** 

**05 OCTOBER 1998** 

Applicant

DIADEXUS LLC

PCT/US99/23252

- The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/US

Commissioner of Patents and Trademarks

Box PCT Washington, D.C. 20231

Facsimile No. (703) 305-3230

Authorized officer

ANNE L. HOLLER.

Telephone No. (703) 308-0196



# **PCT**

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference DEX-0046	FOR FURTHER ACTION	ACTION See Notification of Transmittal of Internation Preliminary Examination Report (Form PCT/IPEA/4		
International application No.	International filing date (day/n	late (day/month/year) Priority date (day/month/year)		
PCT/US99/23252	05 OCTOBER 1999		05 OCTOBER 1998	
International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet.				
Applicant DIADEXUS LLC				
<ol> <li>This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</li> <li>This REPORT consists of a total of sheets.</li> <li>This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</li> <li>These annexes consist of a total of sheets.</li> </ol>				
3. This report contains indications relating to the following items:  I X Basis of the report  II Priority  III Non-establishment of report with regard to novelty, inventive step or industrial applicability  IV Lack of unity of invention  V X Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement  VI Certain documents cited  VII Certain defects in the international application  VIII Certain observations on the international application				
Date of submission of the demand	Date of submission of the demand  Date of completion of this report			
01 MAY 2000 20 FEBRUARY 2001			01	
Name and mailing address of the IPEA/U	<b>I</b>	ized officer	Und ellers for	
Commissioner of Patents and Tradema Box PCT	ì	INE L'HOLLER	LAN SEC	
washington, D.C. 20231				
Form PC1/IPEA/409 (cover sheet) (July		(703)	300-0170	



### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

PCT/US99/23252

I. B	asis of	f the report		
1. Wid	h regard	i to the elements of the intern	national application: *	
х		nternational application as	••	
	1	escription:	5 ,	
X		s <u>1-25</u>		, as originally filed
		NONE		, filed with the demand
			, filed with the letter of	
X		laims: 26-28		
		' <del></del>		, as originally filed
		NONE NONE	, as amended (together with any	
			, filed with the letter of	, filed with the demand
	page		, med with the letter of	
X	the d	rawings:		
ت		NONE		, as originally filed
	pages	NONE		
	pages	NONE	filed with the letter of	
_				
X		quence listing part of the		
	pages	NONE	, filed with the letter of	
		guage of the translation fur	the international application (under Rule 48.3(b) nished for the purposes of international preliminary ex	
3. Wit	h regai	rd to any nucleotide and/o	r amino acid sequence disclosed in the international out on the basis of the sequence listing:	al application, the international
$\mathbf{x}$	contai	ned in the international a	pplication in printed form.	
_			ional application in computer readable form.	
<u> </u>		_	Authority in written form.	
			•	
		•	Authority in computer readable form.	barran di aban diba barran di aba
Ш	interna	atement that the subsequent itional application as filed	ntly furnished written sequence listing does not go has been furnished.	beyond the disclosure in the
	The state	atement that the information urnished.	recorded in computer readable form is identical to the	e writen sequence listing has
4. X	The a	mendments have resulted	in the cancellation of:	
	X	the description, pages	NONE	
	ᄗ	the claims, Nos.	NONE	
		the drawings, sheets/fig	NONE	
5.			some of) the amendments had not been made, since the	ey have been considered to go
		-	indicated in the Supplemental Box (Rule 70.2(c)).**	,
in th	icem <b>e</b> ni	sheets which have been furni ort as "originally filed" and	ished to the receiving Office in response to an invitation u are not annexed to this report since they do not cont	
	•		amendments must be referred to under item 1 and a	nnered to this report

#### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/23252

V.	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability;
	citations and explanations supporting such statement

1.	statement			
	Novelty (N)	Claims	2-4, 7, 8 and 10	YES
		Claims	1, 5, 6 and 9	NO
	Inventive Step (IS)	Claims	2-4, 7 and 8	YES
	• • • • •	Claims	1, 5, 6, 9 and 10	NO
	Industrial Applicability (IA)	Claims	1-10	YES
	Industrial Applicability (IA)			
		Claims	NONE	NO

2. citations and explanations (Rule 70.7)

Claims 1, 5, 6 and 9 lack novelty under PCT Article 33(2) as being anticipated by WO 98/21331 (Incyte Pharmaceuticals, I nc).

Claim 1 is drawn to a method for diagnosing the presence of prostate cancer or a gynecological cancer. Claim 5 is drawn to a method of monitoring the change in state of prostate cancer or a gynecological cancer. The methods of claims 1 and 5 comprise measuring levels of ESBPII. Claim 6 is drawn to any of the methods of claims 1, 2, 3, 4 or 5 wherein the ESBPII comprises SEQ ID NO: 1 or SEQ ID NO: 2. Claims 9 and 10 are drawn to methods of treating prostate or gynecological cancers comprising administering an antibody which binds to ESBPII. The antibody may be conjugated to a cytotoxic agent.

WO 98/21331 discloses an ESBPII protein which is the same as that of SEQ ID NO: 2 (hSBP). WO 98/21331 teaches methods of diagnosing breast cancer by measuring levels of hSBP (page 21, lines 11-32) and of monitoring patients (page 24, lines 5-28). WO 98/21331 also teaches pharmaceutical compositions comprising antibodies specific for SEQ ID NO: 2 (hSBP) for treatment of breast cancer.

Claim 10 lacks an inventive step under PCT Article 33(3) as being obvious over WO 98/21331. Claim 10 modifies claim 9 because the antibody is conjugated to a cytotoxic agent. However, modification of therapeutic a tibodies by adding radiolabels and cytotoxic agents such as a bacterial toxin is well known and does not constitute an inventive step because the use of an antibody specific for SEQ ID NO: 2 is taught by WO 98/21331.

Claims 2-4, 7 and 8 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the methods of diagnosing metastasis, methods of staging, methods of monitoring for the onset of metastasis and methods of imaging prostate cancer.

Claims 1-10 meet the criteria set out in PCT Article 33(4).

(Continued on Supplemental Sheet.)

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### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US99/23252

Supplemental B (To be used whe	ox n the space in any	of the precedir	ng boxes is not s	ufficient)	
Continuation of:					Sheet 10
CLASSIFICATION:  The International Patent Classification (IPC) and/or the National classification are as listed below:  IPC(7): A61K 51/00, 49/00, 39/395; C12Q 1/100, 1/68; GO1N 33/53, 33/567, 33/574 and US Cl.: 424/1.49, 9.1, 130.1, 139.1, 152.1, 178.1, 182.1; 435/4, 6, 7.1, 7.2, 7.21, 7.23, 960					
V. 2. REASONE	D STATEMENTS -	CITATIONS AN	ID EXPLANATIO	NS (Continued):	
	NEW CITATIONS	•••••	-		
NONE					
		-	max.		

# PATENT COOPERATION TREATY

OCT - 2000

Form the			201 1200		
From the INTERNATIONAL PRELIMINARY EXA	AMINING AUTHORITY	<b>,</b>			
To: JANE MASSEY LICATA LAW OFFICES OF JANE MASSEY LICATA 66 E. MAIN STREET			PCT		
MARLTON, NJ 08053			WRITTEN OPINION		
Docket Sy Status Re Docket Bo	port/_		(PCT Rule 66)		
10128	3/00 ANS	Date of Mailing (day/month/year)	2 8 SEP 2000		
Applicant's or agent's file reference		REPLY DUE	vithin ONE months		
DEX-0046		fi	rom the above date of mailing		
International application No.	International filing dat		Priority date (day/month/year)		
PCT/US99/23252	05 OCTOBER 1999		05 OCTOBER 1998		
International Patent Classification (IPC) Please See Supplemental Sheet.	or both national classifi	cation and IPC	·		
Applicant					
DIADEXUS LLC					
<ol> <li>This written opinion is the first</li> <li>This opinion contains indications rel</li> <li>I X Basis of the opinion</li> <li>II Priority</li> </ol>	ating to the following it	ems:	tional Preliminary Examining Authority.		
III Non-establishment of  IV Lack of unity of inver		novelty, inventive ste	p or industrial applicability		
Reasoned statement ur citations and explanations	nder Rule 66.2(a)(ii) with one supporting such sta	h regard to novelty, tement	inventive step or industrial applicability;		
VI Certain documents cit	ed				
VII Certain defects in the	international application	1			
VIII Certain observations of	on the international appl	ication			
3. The applicant is hereby invited to re	ply to this opinion.				
• When? See the time limit indi Authority to grant an	icated above. The applice extension., see Rule 66	cant may, before the o	expiration of that time limit, request this		
How? By submitting a writte For the form and the	en reply, accompanied, language of the amend	where appropriate, b ments, see Rules 66.8	y amendments, according to Rule 66.3.		
For the examiner's of	ortunity to submit amen oligation to consider am munication with the exa	endments and/or area	uments see Rule 66 4 his		
If no reply is filed, the international	il preliminary examinati	on report will be esta	blished on the basis of this opinion.		
4. The final date by which the internation examination report must be establish	onal preliminary	/	$\mathcal{A}^{*}$		
NI					
Name and mailing address of the IPEA/US  Commissioner of Patents and Trademarks Box PCT Washington D.C. 20231  ADME L. HOLLERAN					
Washington, D.C. 20231 Facsimile No. (703) 305-3230		( <sub>2</sub> /	03) 308-0196		
DOTUME HAS		- 5p.:.5116 110. (/I	77) 200-0190		

Form PCT/IPEA/408 (cover sheet) (July 1998)\*

### WRITTEN OPINION

International application No.

PCT/US99/23252

I.	Basis of	the opinion				
1. W	ith regard	to the elements of the interr	estional application.			
Γx		emational application as				
<u> </u>	L. J.	scription:	s originally filed			
X		1-25			•	
		NONE			, as originally filed	
'		NONE			, filed with the demand	
	Pages.		, I	iled with the letter of		
X	the cla	ims:				
-	pages	26-28			, as originally filed	
	pages	NONE	, a:	s amended (together with	any statement) under Article 19	
	pages_	NONE			filed with the domand	
	pages _	NONE	, filed with the	e letter of	, fried with the demand	
	41. 1					
LX.	the dra					
	pages	110117	<del></del>	<del>_</del>	, as originally filed	
	pages _				, filed with the demand	
	pages _	NONE	, file	d with the letter of		
$\mathbf{x}$	the sea	ence listing part of the d	eccrintian:			
لتا			-			
					, as originally filed, filed with the demand	
	pages _	NONE	filed	with the letter of	, filed with the demand	
					nis Authority in the language in which which is:	
	the lang	uage of a translation fur	mished for the purp	oses of international sear	ch (under Rule 23.1(b)).	
				olication (under Rule 48.3		
$\equiv$						
Ш	or 55.3).	age of the translation furn	ished for the purposes	s of international preliminary	examination (under Rules 55.2 and/	
	,			•	•	
3. With	n regard to wn on the	o any <b>nucleotide and/or a</b> basis of the sequence listi	mino acid sequence	disclosed in the international	application, the written opinion was	
		d in the international ap		l 60		
				computer readable form.	•	
_		subsequently to this A				
		subsequently to this A	•			
					go beyond the disclosure in the	
	The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.					
4. X	X The amendments have resulted in the cancellation of:					
	X the	description, pages	NONE			
	X the	claims, Nos.	NONE			
. [	-	drawings, sheets/fig	NONE	· ·	,	
5.	This opini	on has been drawn as if (s	ome of) the amendme	ents had not been made since	e they have been considered to go	
	beyond th	ne disclosure as filed, as in	dicated in the Supple	mental Box (Rule 70.2(c)).	~ usey have occin considered to go	
* Replac	cement she			• • • • • • • • • • • • • • • • • • • •	ion under Article 14 are referred to	

### WRITTEN OPINION

International application No.

PCT/US99/23252

citations and explanations supporting	g such statem	egard to novelty, inventive step or industrial applica nent	wiiiy;
1. statement			
Novelty (N)	Claims	2-4, 7, 8 and 10	YES
	Claims	1, 5, 6 and 9	_ NO
Inventive Step (IS)	Claims	2-4, 7 and 8	VEC
<u>-</u>		1, 5, 6, 9 and 10	_ YES NO
•			
Industrial Applicability (IA)	Claims	1-10	YES
	Claims	NONE	_ NO
2. citations and explanations		•	
Claims 1, 5, 6 and 9 lack novelty under PCT	Article 33(2) as	being anticipated by WO 98/21331 (Incyte Pharmaceuticals,	Inc).
WO 98/21331 also teaches pharmaceutical cor of breast cancer.  Claim 10 lacks an inventive step under PCT because the antibody is conjugated to a cytoto radiolabels and cytotoxic agents such as a bac use of an antibody specific for SEQ ID NO:	Article 33(3) as oxic agent. Hocterial toxin is v		-28). Iment aim 9
Claims 2-4, 7 and 8 meet the criteria set out the methods of diagnosing metastasis, method	n PCT Article	33(2)-(3), because the prior art does not teach or fairly su	
imaging prostate cancer.	s of staging, m	nethods of monitoring for the onset of metastasis and metho	ggest ds of
imaging prostate cancer.  Claims 1-10 meet the criteria set out under Po			ggest ds of
maging prostate cancer.	CT Article 33(4		ggest ods of
Claims 1-10 meet the criteria set out under Po	CT Article 33(4		ggest ods of
Claims 1-10 meet the criteria set out under Po	CT Article 33(4		ggest ods of
Claims 1-10 meet the criteria set out under Po	CT Article 33(4		ggest ods of



#### WRITTEN OPINION

International application No.

PCT/US99/23252

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

#### TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

#### CLASSIFICATION: •

The International Patent Classification (IPC) and/or the National classification are as listed below: IPC(7): A61K 51/00, 49/00, 39/395; C12Q 1/100, 1/68; GO1N 33/53, 33/567, 33/574 and US C1.: 424/1.49, 9.1, 130.1, 139.1, 152.1, 178.1, 182.1; 435/4, 6, 7.1, 7.2, 7.21, 7.23, 960

· Nav

# **PCT**

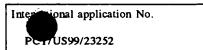
REC'D 0 9 MAR 2001

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

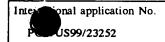
Applicant's or agent's file reference	EOD EUDTUED ACTION	See Notification of Transmittal of International		
DEX-0046	FOR FURTHER ACTION	Preliminary Examination Report (Form PCT/IPEA/416)		
International application No.	International filing date (day/mo	nth/year) Priority date (day/month/year)		
PCT/US99/23252	05 OCTOBER 1999	05 OCTOBER 1998		
International Patent Classification (IPC) Please See Supplemental Sheet.	or national classification and IPC			
Applicant DIADEXUS LLC				
This international preliming     Examining Authority and is	ry examination report has be transmitted to the applicant ac	een prepared by this International Preliminary cording to Article 36.		
2. This REPORT consists of a	total of 4 sheets.			
been amended and are the	panied by ANNEXES, i.e., sheets basis for this report and/or sheet ion 607 of the Administrative In	of the description, claims and/or drawings which have to containing rectifications made before this Authority. structions under the PCT).		
These annexes consist of a to	tal of <u>0</u> sheets.			
3. This report contains indication	s relating to the following item	ns:		
I X Basis of the repor	t			
II Priority				
III Non-establishmen	t of report with regard to nove	lty, inventive step or industrial applicability		
IV Lack of unity of i		11		
V X Reasoned statement citations and explar	under Article 35(2) with regard attions supporting such statemen	to novelty, inventive step or industrial applicability;		
VI Certain documents cited				
VII Certain defects in the international application				
VIII Certain observations				
Date of submission of the demand	Date of	completion of this report		
01 MAY 2000	20 F	EBRUARY 2001		
Name and mailing address of the IPEA/US  Commissioner of Patents and Trademarks  Authorized officer  Ulandal				
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231  ANNE L HOLLERAN				
Facsimile No. (703) 305-3230	Telephor	ne/No. (703) 308-0196		
Form PCT/IPFA/409 (cover sheet) (July	1000			

Form PCT/IPEA/409 (cover sheet) (July 1998) \*



I. Ba	asis	f the report	
1. With	regai	d to the elements of the international applicati	on:*
x	-	international application as originally fi	
=	the	description:	
х		es1-25	, as originally filed
		es NONE	, filed with the demand
			, filed with the letter of
	41		•
X		claims: es 26-28	i-i11 E1-4
			, as amended (together with any statement) under Article 19
		es NONE	, as amended (together with any statement) under Article 19
	-		rith the letter of, mod with the
x	the o	drawings:	
	page		, as originally filed
		s NONE	, filed with the demand
	page	s NONE	, filed with the letter of
(T)	tha a	aguanga liating most of the description.	
X		equence listing part of the description:  1-2	an originally filed
			, as originally filed , filed with the demand
	page	s NONE	, filed with the letter of
	the la	anguage of publication of the internation	ne purposes of international search (under Rule 23.1(b)).  nal application (under Rule 48.3(b)).  purposes of international preliminary examination (under Rules 55.2 and/
3. With	h rega limina	ard to any <b>nucleotide and/or amino acid</b> ary examination was carried out on the b	-
X	conta	ined in the international application in	printed form.
		together with the international applicat	
===		shed subsequently to this Authority in v	
=		shed subsequently to this Authority in c	
			•
Ш	intern	national application as filed has been furn	written sequence listing does not go beyond the disclosure in the ished.
	The s been	tatement that the information recorded in confurnished.	omputer readable form is identical to the writen sequence listing has
4. X	The .	amendments have resulted in the cance	llation of:
	X	the description, pages NONE	
	X	the claims, Nos. NONE	<del></del>
	$\overline{\mathbf{x}}$	the drawings, sheets/fig NONE	<del></del>
5.			nendments had not been made, since they have been considered to go
L)		and the disclosure as filed, as indicated in the	·
in th	cemer	nt sheets which have been furnished to the reco ort as "originally filed" and are not annex	eiving Office in response to an invitation under Article 14 are referred to ed to this report since they do not contain amendments (Rules 70.16
			nust be referred to under item 1 and annexed to this report.

#### RY EXAMINATION REPORT



l applicability;
YES
NO
YES
NO
YES
NO
_

#### 2. citations and explanations (Rule 70.7)

Claims 1, 5, 6 and 9 lack novelty under PCT Article 33(2) as being anticipated by WO 98/21331 (Incyte Pharmaceuticals, I nc).

Claim 1 is drawn to a method for diagnosing the presence of prostate cancer or a gynecological cancer. Claim 5 is drawn to a method of monitoring the change in state of prostate cancer or a gynecological cancer. The methods of claims 1 and 5 comprise measuring levels of ESBPII. Claim 6 is drawn to any of the methods of claims 1, 2, 3, 4 or 5 wherein the ESBPII comprises SEQ ID NO: 1 or SEQ ID NO: 2. Claims 9 and 10 are drawn to methods of treating prostate or gynecological cancers comprising administering an antibody which binds to ESBPII. The antibody may be conjugated to a cytotoxic agent.

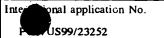
WO 98/21331 discloses an ESBPII protein which is the same as that of SEQ ID NO: 2 (hSBP). WO 98/21331 teaches methods of diagnosing breast cancer by measuring levels of hSBP (page 21, lines 11-32) and of monitoring patients (page 24, lines 5-28). WO 98/21331 also teaches pharmaceutical compositions comprising antibodies specific for SEQ ID NO: 2 (hSBP) for treatment of breast cancer.

Claim 10 lacks an inventive step under PCT Article 33(3) as being obvious over WO 98/21331. Claim 10 modifies claim 9 because the antibody is conjugated to a cytotoxic agent. However, modification of therapeutic antibodies by adding radiolabels and cytotoxic agents such as a bacterial toxin is well known and does not constitute an inventive step because the use of an antibody specific for SEQ ID NO: 2 is taught by WO 98/21331.

Claims 2-4, 7 and 8 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest the methods of diagnosing metastasis, methods of staging, methods of monitoring for the onset of metastasis and methods of imaging prostate cancer.

Claims 1-10 meet the criteria set out in PCT Article 33(4).

(Continued on Supplemental Sheet.)



INTERNATIONAL PRELI	RY EXAMINATION REPORT	P. US99/23252
Supplemental Box (To be used when the space in any	of the preceding boxes is not sufficient)	
Continuation of: Boxes I - VIII		Sheet 10
CLASSIFICATION:  The International Patent Cla IPC(7): A61K 51/00, 49/00, 39/395; 139.1, 152.1, 178.1, 182.1; 435/4, 6	ssification (IPC) and/or the National classifica; C12Q 1/100, 1/68; GO1N 33/53, 33/567, 33, 7.1, 7.2, 7.21, 7.23, 960	ation are as listed below: 3/574 and US Cl.: 424/1.49, 9.1, 130.1,
V. 2. REASONED STATEMENTS -	CITATIONS AND EXPLANATIONS (Conti	nued):
NEW CITATIONS NONE		

THIS PAGE DI ANK (USPTO)

FEB 14 2000

From the INTERNATIONAL SEARCHING AUTHORITY

To: JANE MASSEY LICATA				
LAW OFFICES OF JANE MASSEY LICATA	PC-1			
66 E. MAIN STREET MARLTON, NJ 08053				
WARETON, 143 00033	NOTIFICATION OF TRANSMITTAL OF			
Docket System	THE INTERNATIONAL SEARCH REPORT			
Status Fleport	OR THE DECLARATION			
DOCKEL DOOK	(PCT Rule 44.1)			
3/11(00/100)	(1 C1 Rule 44.1)			
· ·	Date of Mailing (day/month/year) 11 FEB 2000			
Applicant's or agent's file reference	FOR HUNDYING ACTION			
DEX-0046	FOR FURTHER ACTION See paragraphs 1 and 4 below			
International application No.	international filing date			
PCT/US99/23252	(day/month/year) 05 OCTOBER 1999			
Applicant				
DIADEXUS LLC	·			
	al search report has been established and is transmitted herewith.			
Filing of amendments and statement under Artic The applicant is entitled, if he so wishes, to amend	the claims of the international application (see Rule 46):			
When? The time limit for filing such amends	scats is normally 2 months from the date of transmittal of the			
international search report, however, for	more details, see the notes on the accompanying sheet.			
Where? Directly to the International Bureau of V				
34, chemin des Colombettes 1211 Geneva 20, Switzerland				
Facsimile No.: (41-22) 740.14.35				
For more detailed instructions, see the notes on	the accompanying sheet.			
2. The applicant is hereby notified that no international Article 17(2)(a) to that effect is transmitted herewith.	I search report will be established and that the declaration under			
3. With regard to the protest against payment of (an)	additional fee(s) under Rule 40.2, the applicant is notified that:			
the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.				
no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.				
4. Further action(s): The applicant is reminded of the fol	lowing:			
the applicant wishes to avoid of postnone publication.	onal application will be published by the International Bureau. If a notice of withdrawal of the international application, or of the provided in rules 90 bis 1 and 90 bis 3, respectively, before the al publication.			
Within 19 months from the priority date, a demand for in	ternational preliminary examination must be filed if the applicant (til 30 months from the priority date (in some Offices even later).			
Within 20 months from the priority date, the applicant must	perform the prescribed acts for entry into the national phase before			
Name and malling add.				
Name and mailing address of the ISA/US  Commissioner of Patents and Trademarks	Authorized offer			
Box PCT Washington, D.C. 20231	AWNE HOLLERAN			
Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196			

### PATENT COOPERATION TREATY

### **PCT**

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference DEX-0046	FOR FURTHER ACTION	see Notification of (Form PCT/ISA/220	Transmittal of International Search Report ) as well as, where applicable, item 5 below.
International application No.	International filing date	(day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/US99/23252	05 OCTOBER 1999		05 OCTOBER 1998
Applicant DIADEXUS LLC			
This international zearch report has bee according to Article 18. A copy is bein  This international search report consists  X It is also accompanied by a companied by a c	g transmitted to the Internation of a total of $\frac{\mathcal{L}}{\mathcal{L}}$ sheets.	ational Bureau.	thority and is transmitted to the applicant
1. Certain claims were found	unsearchable (See Box I)	).	
2. Unity of invention is lacking	g (See Box II).		
3. X The international application international search was carried	contains disclosure of a ed out on the basis of the	nucleotide and/or sequence listing	amino acid sequence listing and the
X f	iled with the international	application.	
	umished by the applicant	separately from the	international application,
	but not accor	mpanied by a stateme	nt to the effect that it did not include matter e international application as filed.
	ranscribed by this Authorit		
	he text is approved as sub- he text has been establishe reflect claimed subje	d by this Authority	
New Title: A NOVEL M TREATING GLYNECOL 5. With regard to the abstract,	METHOD OF DIA OGICAL AND PRO	GNOSING, M DSTATIC CAN	IONITORING, STAGING AND ICERS
N :	ie ieki is approved as sub:	nitted by the annlice	ant
the distribution of the di	ne text has been establishe	d, according to Rule may, within one m	38.2(b), by this Authority as it appears onth from the date of mailing of this
6. The figure of the drawings to be pu	blished with the abstract is	<b>::</b>	
Figure No.	s suggested by the applica		
<b>∺</b> .	ecause the applicant failed		None of the figures.
<b>—</b>	ecause this figure better ch		

International application No.

PCT/US99/23252

A. CLASSIFICATION OF SUBJECT MATTER IPC(6) :Please See Extra Sheet.		
US CL :Please See Extra Sheet.		
According to International Patent Classification (IPC) or to B. FIELDS SEARCHED	both national classification and IPC	
Minimum documentation searched (classification system fol	lowed by classification and tall	
	•	
U.S.: 424/1.49, 9.1, 130.1, 139.1, 152.1, 178.1, 182.1;	435/4, 6, 7.1, 7.2, 7.21, 7.23, 960	
Documentation searched other than minimum documentation	to the extent that such documents are included	in the fields searched
Electronic data base consulted during the international searc	h (name of data base and, where practicable	s search terms used)
US PATENTS (EAST/BRS), MEDLINE, EMBASE, BIOS search terms: esbp, espbii, hesfii, hesf, lipophilin, estramus	IS, CAPLUS	
C. DOCUMENTS CONSIDERED TO BE RELEVAN	Т	
Category* Citation of document, with indication, when	e appropriate, of the relevant passages	Relevant to claim No.
X,P WO 98/56248 A1 (SMITHKLINE 17 December 1998, pages 9 and 16	BEECHMAN CORPORATION)	1, 5, 6 and 9
W.D.		10
Y,P		
X WO 98/21331 A1 (INCYTE PHAR 1998, pages 21, 24, 26-28, 31 and	WO 98/21331 A1 (INCYTE PHARMACEUTICALS INC.) 22 May 1998, pages 21, 24, 26-28, 31 and 41.	
		10
Y		
X Further documents are listed in the continuation of Bo	x C. See patent family annex.	
Special categories of cited documents:		
A* document defining the general state of the art which is not consider to be of particular relevance	date and not in conflict with the applied the principle or theory underlying the	cation but cited to understand
earlier document published on or after the international filing date  document which may throw doubts on priority claim(s) or which	is when the document is taken alone	e claimed invention cannot be red to involve an inventive step
cited to establish the publication date of another citation or othe special reason (as specified)	er "Y" document of particular relevance; the	claimed invention cannot be
O* document referring to an oral disclosure, use, exhibition or oth means	considered to involve an inventive er combined with one or more other such being obvious to a person skilled in the	documents, such combination
P* document published prior to the international filing date but later the the priority date claimed		
Date of the actual completion of the international search	Date of mailing of the international sea	rch report
12 JANUARY 2000	1/1 FEB 200	0
Name and mailing address of the ISA/US  Commissioner of Patents and Trademarks	Authorized officer	- co.
Box PCT Washington, D.C. 20231	ANNE IL HOLLERAN	Collin
facsimile No. (703) 305-3230	Telephone No. (703) 308-0196	/

International application No. PCT/US99/23252

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT				
Category*	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.	
Y	Database EMBASE on STN, Elsevier Sci. B.V., SHIINA Immunohistochemical analysis of estramustine binding with particular reference to proliferative activity in hum carcinoma, abstract, Prostate, 1997, Vol. 32, No. 1, page	1, 3, 5 and 6		
A	PARKER et al. Prostatic steroid binding protein: gene and steroid binding. Nature. 01 July 1982, Vol. 298, pa see entire document.	duplication ges 92-94,	1-6	
A,P	ZHAO et al. Lipophilins: Human peptides homologous prostatein. Biochem. Biophys. Res. Commun. 1999, Vopates 147-155, especially page 147.	to rat l. 256,	1-6	
			·	
	-			

International application No. PCT/US99/23252

A. CLASSIFICATION OF SUBJECT MATTER: IPC (6):

A61K 51/00, 49/00, 39/395; C12Q 1/100, 1/68; GO1N 33/53, 33/567, 33/574

A. CLASSIFICATION OF SUBJECT MATTER: US CL  $\,:\,$ 

424/1.49, 9.1, 130.1, 139.1, 152.1, 178.1, 182.1; 435/4, 6, 7.1, 7.2, 7.21, 7.23, 960

Form PCT/ISA/210 (extra sheet)(July 1992)★